

# Toxicological Studies of Shale Oils, Some of Their Components, and Commercial Products

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Estonian shale oil contains about 25–30% phenols, and their action determines the toxicity of shale oils. The clinical symptoms of intoxication are rather similar, regardless of route of administration. Due to neurotropic action, the coordination of movements is impaired, and clonic and tetanic convulsions, paresis and paralysis of extremities, and narcosis are observed. In subacute and chronic toxicity tests, dysfunction of the central nervous system was found. In long-term (4–6 month) experiments, changes in liver and kidney function were found. Shale oil has gonadotropic activity and causes changes in the sexual cycle as well as diminution of the number of primordial follicles in the ovaries or a decrease in the quantity of normal spermatogonia in testicular germinal epithelium. Shale oils produce local irritation of skin and mucous membranes. Shale oil can induce sensitization of the organism after repeated administration.

The results of acute intoxication tests have proved that volatile and nonvolatile phenol fractions, isomeric dimethylphenols, and 5-methylresorcinol, must be characterized as moderately toxic substances; the LD<sub>50</sub> ranges from 501 to 1500 mg/kg.

The clinical symptoms of acute intoxication are similar for all studied phenols (restlessness, unsteadiness, clonic tremor, paresis and paralysis of extremities, and death).

In spite of the moderate toxicity of phenols in acute experiments, repeated administration of small doses can cause different changes in the nervous system and internal organs of experimental animals.

For all the phenols studied, the maximum allowable concentration in water was limited by their effect on the organoleptic properties of water. The nonactive dose for warm-blooded animals is from 100 to 3000 times the threshold limit value of phenols on the basis of their organoleptic properties.

The effect of commercial products of oil shale industry is generally determined by the toxicity of the main components: water-soluble oil shale phenols.

Estonia possesses the largest oil shale mines and oil shale processing plants of the world. A large proportion (about two thirds) of oil shale output is used directly as solid fuel in power stations. The rest is thermally processed, yielding mainly oils, which are used as liquid fuel and raw material for the chemical industry.

For over 20 years the Institute of Experimental and Clinical Medicine of the Ministry of Health of the Estonian S.S.R. has been carrying out investigations in industrial hygiene, occupational pathology, and toxicology of oil shale products. Of these, mainly shale oils and various phenols have been studied.

The industry produces two main varieties of shale oils. Low-temperature (500°C) processing is carried

out in tunnel ovens, generators, and in solid heat carrier departments. The oils contain various hydrocarbons (paraffins, naphthenes, olefins, aromatic compounds), neutral and acidic oxygen compounds (phenols, etc.), as well as sulfur- and nitrogen-containing compounds. The high-temperature oil (pyrolysis at 1000–1200°C) is produced in chamber ovens. This oil differs from the low-temperature oils in containing considerable proportions (up to 53%) of aromatic compounds.

From the toxicological point of view, the oils, being complex mixtures of the representatives of different groups of chemicals, can show diverse toxic effects depending on the route of administration (inhalation of volatiles, skin application, etc.).

The toxicity of low-temperature shale oils and the intoxication hazard in occupational conditions depends, according to Jänes (1) and Blinova et al. (2) on the chemical and physicochemical properties of

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these oils. The fractions boiling at lower temperatures contain up to 70% unsaturated hydrocarbons. In the high-temperature (heavy) fractions, the proportion of phenols and neutral oxygen compounds increases. Therefore the light and heavy fractions have to be considered separately in evaluating the toxicity of shale oils.

The light fractions of low-temperature shale oils are less toxic than the heavy fractions. For example, in inhalation experiments in mice, the LD<sub>50</sub> of the volatile components of light oil of the solid heat carrier plant for the intermediate to heavy oil is 63 ± 3 mg/l., and 16 ± 2 mg/l., respectively.

On the other hand, at 20°C the light fractions are up to 50 times as volatile than heavy fractions, and for this reason the real intoxication hazard due to low boiling fractions is much higher (Table 1).

The proportion of light fractions in oils processed in different departments varies considerably. It is, for example, higher in the tunnel oven oil and in the solid heat carrier department oil. The toxicity of various oils depends on these variations in composition. Volatile components of the chamber oven oil and the generator oil are, for example, more toxic than components of the oils mentioned before (Table 1).

Estonian shale oil contains about 25–30% phenols. Although both main components of oils, the hydrocarbons and the phenols, possess toxic properties, the activity of the phenols determines the toxicity of the shale oil.

The clinical symptoms of intoxication in experimental animals, even if various routes of administration are used, are rather similar. Due to the neurotropic action the coordination of movements is impaired; clonic and tetanic convulsions, paresis and paralysis of extremities, and narcosis are observed. In subacute and chronic toxicity tests, dysfunction of the central nervous system can be found: typical findings are a decrease in chronaxia, reduction of the ability to summarize subthreshold

impulses, and decline in the neuromuscular excitability.

Changes in other organs and systems can also be found in long-term (4–6 month) experiments. Anemia and leukopenia have been observed, as well as decreases in the activity of catalase and peroxidase. The blood serum sulfhydryl (–SH) content and the glucose level are reduced. The antitoxic activity and protein synthesis in the liver are decreased as shown by the experimental prolongation of hexenal narcosis, and the blood serum albumin level is decreased. Kidney function also undergoes certain changes: the level of residual N in blood is increased, albuminuria, ketonuria and glycosuria can occur, and the urinary excretion of phenols is increased.

Morphological examination of internal organs of experimental animals shows degenerative changes in liver and glomerular proliferation of endothelial cells.

Shale oil also exerts gonadotropic action, as demonstrated in experiments on rats (3). The peroral administration of oil (15 days, 10 g/kg of body weight per day) induces the lengthening of the estral (diestral) cycle. In doses of 0.1 g/kg per day for 4 months, the oil causes changes in the sexual cycle as well as a diminution of the number of primordial follicles in the ovaries or a decrease in the quantity of normal spermatogonia in the testicular germinal epithelium.

Locally, shale oils produce irritation of skin and mucous membranes. In acute experiments in the rat (application to skin for 3 hr), shale oil causes a decrease in the threshold of neuromuscular excitability, the shortening of the time spent climbing up a vertical stick, and an increase in the frequency of respiration. Fatty degeneration of liver cells and hyperplastic changes in the spleen follicles have been observed.

It has also been demonstrated that shale oils can induce the sensitization of the organism after re-

Table 1. Boiling temperature, volatility, and toxicity for mice of various shale oils.

Oil	Boiling point, °C	Volatilization at 350°C, vol %	LD <sub>50</sub> , mg/l.	Toxicity coefficient
Chamber oven oil	150–180	30.3–62.0	39 ± 1.5	1.0
Solid heat carrier department oil light fraction	73	87.0	63 ± 3.0	0.5
Solid heat carrier oil, intermediate heavy fraction	189	50.0	16 ± 2.0	2.1
Tunnel oven oil, intermediate fraction	192–215	76.5	66 ± 3.5	0.4
Generator oil	130	47.0	27 ± 1.4	1.2
Diesel oil fraction	180	96.0	15 ± 0.3	2.6

peated administration.

Experimental data have been confirmed by clinical observations. Kahn (4) reported moderate intoxication in 215 shale oil industry workers. Most findings were subjective, including such symptoms as headaches, fatigue, irritability, sleep disorders, hyperhidrosis etc. Signs like increase in urinary excretion of phenols and glucuronic acid, eosinophilia, and immunodepression have also been observed. These changes were less correlated with the length of exposure of workers, depending more on individual susceptibility. The working ability of workers was usually not impaired.

Loogna and Hering (5) demonstrated the occurrence of allergic dermatoses due to shale oil in workers.

The toxic properties of shale oils are due to different chemical compounds. Toxicity can be approximately estimated from boiling temperatures and the contents of phenols. It must be mentioned that toxic and carcinogenic properties have no common denominator; for example, in mice the chamber oven oil is strongly carcinogenic but moderately toxic, the intermediate fraction of the solid heat carrier department oil is moderately carcinogenic but highly toxic, and the generator oil is moderately carcinogenic and moderately toxic.

Investigations of biologic activity, especially on the character and level of toxicity of oil shale phenols, were carried out at our Institute in order to determine and recommend the threshold limit value of phenols in bodies of water.

The phenols in oil shale industry wastewater are a mixture which contains 85–90% diphenols (non-volatile) and 10–15% monophenols (volatile) (6).

The volatile phenol fraction is a dark brown viscous fluid with a special odor. It is soluble in water and boils at 182–270°C. The odor of volatile phenols was classified as objectionable, the taste at their low concentrations as sweetish, at higher concentrations as bitterish and obnoxious.

The study of the effect of volatile phenols on the organoleptic properties of water has shown that the level of objectionable odor is set at 0.05 mg/l. The chlorination of volatile phenols leads to the formation of chlorophenols. The level of the odor of chlorophenols was fixed at 0.025 mg/l. On sanitary regulation of experimental water bodies (self-purifying processes) volatile phenols do not act at concentrations less than 0.5 mg/l. At a concentration of 1 mg/l. volatile phenols hinder the process of biochemical oxidation.

Acute, subacute, and chronic toxicologic experiments were carried out to study the action of volatile phenols on warm-blooded animals.

The daily oral administration of volatile phenols

to white rats and rabbits for 7 months showed that only the largest of all tested doses (0.1 LD<sub>50</sub> or 38.6 mg/kg) causes some functional changes, i.e., increase in blood pressure, loss of weight, and some histological changes of the internal organs (parenchymatous dystrophy of liver, kidneys, and spleen). The conclusion was drawn that this dose of volatile phenols must be considered as an active one.

The administration of 0.01 and 0.001 LD<sub>50</sub> of volatile phenols did not cause such changes.

The nonvolatile phenol fraction is a tarlike, dark brown mixture with a boiling range of 271–315°C, which rather slowly dissolves in cold water. By studying the effect of nonvolatile phenols on the organoleptic properties of water it was found that their threshold limit value in water was limited by their color and according to it their level in water bodies was set at a concentration of 0.41 mg/l. for water bodies used for the water supply of cities and at 0.26 mg/l. for sea water. On the hygienic regulation of water bodies the nonvolatile phenols play a role only if their concentration is higher than 0.5 mg/l.

Long-term studies in experimental animals resulted in the following conclusions: daily oral administration of 63.3 mg/kg of body weight (0.1 LD<sub>50</sub>) nonvolatile phenols for 7 months causes loss of weight, increase in blood pressure, changes in peripheral blood, and parenchymatous dystrophy of the internal organs of experimental animals. A dose of 0.01 LD<sub>50</sub> (6.33 mg/kg body weight) turned out to be inactive. The last dose, which corresponds to 127 mg/l. of water for man, was nearly 1000 times the threshold limit value of nonvolatile phenols determined by their effect on the organoleptic properties of water.

Lille and Kundel (7), studying the phenols in oil shale wastes by gas chromatography, have determined that the nonvolatile phenol fraction consists of the alkyl derivatives of resorcinol and the majority of them represents 5-methylresorcinol (orcinol) (5-MR). The volatile fraction of oil shale phenols consists of hydroxybenzene (carbolic acid), cresols, xlenols, and higher phenols, which are represented by  $\alpha$ - and  $\beta$ -naphthol and others. The content of xlenols—*isomeric dimethylphenols* (DMP)—is rather large.

This explains the great interest which environmental health scientists and toxicologists take in *isomeric DMP* and in 5-MR. The toxicological and biological activity of these phenols has not yet been studied as to their activity in water bodies; therefore our further investigations were dedicated to the problem of characterizing the above-mentioned phenols.

In order to determine the conditions of activity in

experimental animals, isomeric DMP compounds in different doses were administered orally to white rats over an 8-month period.

The long-term experiments (results presented in Table 2) indicate that the isomeric DMP compounds in the dose of 0.02 LD<sub>50</sub> are active.

The administration of 0.6 mg/kg 2,6-DMP and 1.4 mg/kg 3,4-DMP did not have any specific effect on the experimental animals in comparison with the control rats.

The toxicity level of the isomeric DMPs by their activities on the health regulation of water bodies was fixed at a concentration of 0.5 mg/l. for 3,4- and 3,5-DMP and at 2.5 mg/l. for 2,6- and 2,5-DMP. The safety limit of the isomeric DMP in water can be set by its organoleptic properties at 0.1 mg/l.

As mentioned above, the nonvolatile fraction of oil shale phenols contains large quantities of 5-MR, which is the only nonvolatile phenol that has been isolated from oil shale phenols in pure form.

It was determined that the influence of 5-MR on the color of water is the most important one of its organoleptic properties. The threshold limit value of 5-MR in water bodies was fixed at 1 mg/l. for primary water bodies (reservoirs) and 5 mg/l. for the sea. At a concentration of 1 mg/l. 5-MR some action on biochemical oxidation may be observed.

The results of an 8-month experiment with vari-

ous doses of 5-MR on white rats are presented in Table 2. The daily oral administration of 33.8 mg/kg 5-MR caused various changes in the white rat. A daily dose of 8.4 mg/kg (0.01 LD<sub>50</sub>) 5-MR, administered over an 8-month period, caused only a very slight inhibition of reflexes of experimental animals and was characterized as a nontoxic dose.

On comparing all the results of the experiment with 5-MR it must be emphasized that the level of toxicity of 5-MR in water bodies has been determined by its effect on the organoleptic properties (color) of water. The threshold limit value was recommended at a level of 1.0 mg/l, which is smaller by nearly a factor of 170 than the nontoxic dose for warm-blooded animals.

On summing up the data characterizing the biological activity of the studied oil shale phenols, the following conclusion may be drawn.

The results of an acute intoxication test have proved that volatile and nonvolatile phenol fractions, isomeric DMPs and 5-MR, according to the classification of Zaugolnikov et al. (8), must be characterized as moderately toxic substances, i.e., having LD<sub>50</sub> from 501 to 1500 mg/kg.

The clinical symptoms of an acute intoxication are similar for all studied phenols (restlessness, unsteadiness, clonic tremor, pareses and paralysis of extremities, and death).

Table 2. Results of long-term oral administration of phenols in white rat.<sup>a</sup>

Test	2,6-DMP		3,4-DMP			5-MR	
	0.02 LD <sub>50</sub> (6 mg/kg)	0.002 LD <sub>50</sub> (0.6 mg/kg)	0.2 LD <sub>50</sub> (14 mg/kg)	0.002 LD <sub>50</sub> (1.4 mg/kg)	0.04 LD <sub>50</sub> (33.8 mg/kg)	0.01 LD <sub>50</sub> (8.4 mg/kg)	0.002 LD <sub>50</sub> (1.7 mg/kg)
Weight of animals	+	0	+	0	+	0	0
Peripheral blood analyses	0	0	+	0	+	0	0
Blood pressure	+	0	+	0	0	0	0
Blood pressure after adrenalin injection	0	0	+	0	0	0	0
SH groups of blood serum	+	0	0	0	±		0
Protein fractions of blood serum	0	0	0	0	±		0
Antitoxic activity of liver	0	0	0	0	0	0	0
Excretion of free and conjugated phenols in urine	0	0	0	0	+	0	0
Effect on central nervous system	0	0	0	0	+	±	0
Ability to summarize subthreshold impulses	0	0	0	0	+	0	0
SH groups in internal organs	+	0	+	0	±	0	0
Vitamin C in adrenals	0	0	0	0	+	0	0
Pathomorphological changes of internal organs	+	0	+	0	+	0	0

<sup>a</sup> Symbols: (+) significant changes; (±) nonsignificant changes; (0) no changes.

In spite of the moderate toxicity of phenols in the acute experiment, the repeated oral administration of small doses can cause different changes in the nervous system and internal organs of experimental animals.

Although the volatile phenols (monophenols) are a little more active than the nonvolatile diphenols, there is no great difference in the dose of phenol which causes changes in chronic intoxication tests in warm-blooded animals.

For all the phenols studied, the threshold limit value in water was limited by their effect on the organoleptic properties of water (odor for volatile and color for nonvolatile phenols). The nonactive dose for warm-blooded animals varies from 100 (isomeric DMPs) to 3000 (volatile phenolfraction) times the threshold limit value of phenols by their organoleptic properties.

The variety of chemical products which are manufactured from shale oils and phenols is rather extensive. This assortment consists of fuel products (shale oil, fuel oil and shale oil petrol), various kinds of varnishes and mastics, Kukersol varnishes, LSP-1, bitumen-kukersol, mastic, and SFM-2 and DFK-10 pitches, which are used as solvents and glue, and also as materials for the electric, radiotechnical, and rubber industries (oil shale epoxide pitch, phenol pitch, printing ink). Moreover, a number of products have specific uses: SRV-1, a stimulator of plant growth; oil shale tanning stuff for processing leather; phenolin for ringworm treatment, etc.

The above are either thermal processing products of oil shale and oils (shale oil petrol) or mixtures of some fractions of shale oils and phenols (the bitumen-kukersol mastic) or condensation products with other chemical compounds (SFM-2 pitch). Formaldehyde is most often used as a chemical auxiliary, and occasionally epichlorohydrin or colophony are also applied. The volatile compounds of shale oil and phenol products in the air have a toxic effect on the organism.

The effect of the commercial products of the shale oil industry is generally determined by the toxicity of its main components. Moderate or weak toxic symptoms are associated with the effects on the nervous system and in the case of an acute effect the symptoms of narcotic and irritant action predominate. The "P" printing ink and the SFM-2 pitch belong to the least toxic substances. Their steam-gas mixture does not kill experimental animals.

The intensity of the effect of investigated substances on the skin correlates with the degree of toxicity by inhalation. A skin resorption effect was most clearly evident in the case of the Kukersol

varnish and the oil shale solvent. The sharp and unpleasant smell of the products are produced from oil shale as well as the prolonged migration of volatile components into the surrounding air makes it necessary to limit their utilization in the construction of dwellings.

The real hazard of commercial products from oil shale increases under heating. Heating takes place in industry, which produces those products, and in many cases of their utilization.

The introduction of the gas-chromatographic method, which was used in the analysis of the volatile components of water-soluble oil shale phenols, enables us to distinguish more exactly the ingredients of the volatile components of the products investigated. For some of the volatile components of the mixtures investigated, safety limits have been worked out and the question of their threshold limit value will be examined, depending on the character of the action of separate ingredients of this mixture: independent, one-directional, and mixed. One of the possibilities for establishing safety limits in the case of a complex mixture is to do it according to the major component of mixtures (9). The main method to combat the toxic effect of shale oils and phenols is to work out safety limits for them in the environment, to apply technological, technical, and occupational health measures as well as medical, individual, and organizational measures of prevention. Long experience has shown that only combined prevention enables us to guarantee security while working with shale oils and phenols.

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